files were quantified using glyoxylic acid (SPG)-induced histofluorescence and immunohistochemical staining of neuropeptide Y (NPY), a sympathetic neurotransmitter which is co-released with NE.

	Control		Norepinephrine	
	Vits	Placebo	Vits	Placebo
Plasma NE	0.38 ± 0.09	0.50 ± 0.05	1.78 ± 0.28	2.08 ± 0.46
NE uptake	64.9 ± 5.7	65.0 ± 7.8	57.8 ± 6.2	43.1 ± 5.2*+
SPG	137.8 ± 11.9	140.3 ± 10.1	125.5 ± 12.1	88.4 ± 8.4*+
NPY	87.9 ± 6.8	99.3 ± 4.3	102.6 ± 7.4	45.9 ± 3.1*+

(*$p \leq 0.05$ versus control group; +$p \leq 0.05$ versus NE+vits group)

Antioxidants attenuated the decrease in cardiac NE uptake activity and loss of sympathetic neurotransmitters caused by excess NE. These findings implicate NE-derived oxygen free radicals in cardiac noradrenergic dysfunction and thus, suggest a potentially therapeutic role for antioxidant vitamins in CHF.

1083-117 The Endogenous Natriuretic Peptide System Modulates Diastolic Function in Experimental Heart Failure

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Atrial and brain natriuretic peptides (of myocyte origin) and C-type natriuretic peptides (of endothelial origin) are vasoactive peptides whose production by the heart is enhanced in heart failure (HF). Natriuretic peptide (NP) receptors have been demonstrated on LV myocytes and in-vitro studies have suggested that cGMP, the NP second messenger, has effects on myocardial function. Therefore, we hypothesized that the endogenous NP system acts as an autocrine/paracrine system to modulate LV function in HF. To test this hypothesis, HS-142-1 (HS), a specific antagonist of the NP receptors, was infused into the coronary arteries in 5 dogs with chronic HF produced by rapid ventricular pacing at doses designed to produce selective blockade of the intracardiac NP system without systemic effects. Heart rate was controlled by atrial pacing during the infusion. The time constant of LV relaxation (Tau), the time to the onset of LV relaxation (t), mean aortic pressure (mAoP), LV end-diastolic pressure (LVEDP) and peak + dP/dt were measured (*$p \leq 0.05$ vs Control, #$p \leq 0.05$ vs HS dose 1)

	Control	HS dose 1	HS dose 2
mAoP (mmHg)	76 ± 6	79 ± 7	83 ± 10
LVEDP (mmHg)	15 ± 6	16 ± 8	17 ± 6
Peak ± dP/dt (mmHg/s)	1147 ± 212	1199 ± 238	1202 ± 244
Tau (ms)	39 ± 7	45 ± 7*	49 ± 8*#
t (ms)	228 ± 12	238 ± 15*	243 ± 16*

Antagonism of the intracardiac NP system in HF prolonged t and Tau without effects on loading conditions or inotropic function.

Conclusions: In HF, the activated endogenous NP system functions in the heart as an autocrine/paracrine system to enhance LV diastolic function by accelerating LV relaxation These data indicate that the NP system is an important local regulator of cardiac function in HF.

1083-118 The Synergistic Effects of Vitamin E and Selenium on Cardiac Antioxidant Levels in a Model of Iron Overload Cardiomyopathy

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Iron overload cardiomyopathy is a prototype of restrictive cardiomyopathy, and is a common cause of heart failure in young patients worldwide. Oxygen free radical (OFR) production may be pathogenic in heart failure of diverse etiology, including iron overload cardiomyopathy. The myocardium has several intrinsic antioxidants to defend against free radicals, including glutathione peroxidase (GPx), selenium (Se) and vitamin E (Vit E). The deficiencies of the latter 2 species are known to cause heart failure. We determined whether chronic supplementation of Vit E and Se can improve myocardial antioxidant defenses in a model of iron overload cardiomyopathy. Iron overload state was created in $B6D2F_1$ mice by iron dextran injection (5 mg i.p.) daily for 4 weeks. The animals were simultaneously randomized to receive Vit E (α-tocopherol 40 mg i.p.) or Se (sodium selenite 1 ppm p.o.) supplementation individually or both together (Vit E+Se) for 4 weeks (n = 20), vs. D10W p.o. as controls (n = 5). The hearts were harvested for determination of GPx (μmol/L) and SE levels (nmol/L). All data presented as mean ± SD:

	Control	Vit E	Se	Vit E + Se
GPx	162 ± 98	152 ± 72	175 ± 66	346 ± 126**
Se	87 ± 28	98 ± 31	175 ± 74	725 ± 968**

**$p < 0.001$ compared to control or individual Vit E & Se groups.

We conclude that vitamin E and selenium may function synergistically in the myocardium to provide important antioxidant defense mechanisms against free radical damage, such as found in iron overload and heart failure. These elements may also have therapeutic implications in these conditions.

1083-119 Angiogenic Factors Basic Fibroblast Growth Factor and Angiogenin in Advanced Heart Failure Patients

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There are many data which support that in advanced heart failure (HF) occurs neovascularisation and hyperplasia of cardiac myocytes both disproportionate to the hypertrophy. Basic Fibroblast Growth Factor (bFGF), a multifunctional polypeptide which has been localised to adult cardiac myocytes in vitro, has angiogenic properties and stimulates proliferation of cardiac myocytes, endothelial cells etc. Angiogenin (ANG), a non glycosylated polypeptide, so named for its strong ability to induce new blood vessel growth, but its precise role in heart diseases has not yet been well clarified. The aim of our study was to investigate any possible role of bFGF and ANG in patients with heart failure. We studied 50 patients with HF, 41 men, mean age 60 years, and 9 women, mean age 66 years, of different aetiology – coronary heart disease (CHD) 23/50, dilated cardiomyopathy (DCM) 11/50, valvulopathy (VHD) 14/51-, and all classes of NYHA (Class I 8/50, Class II 6/50, Class III 14/50, Class IV 22/50) and compared to 21 healthy controls (17 men and 4 women age-matched). Patients with acute or chronic inflammatory disease, malignancies, collagen disease, thyroid, renal or liver disease, hypertension or diabetes mellitus have been excluded from our study. Before sampling patients were clinically stable and off medication, except diuretics, for a period of 5 days. Samples were measured by relevant ELISA kits. For the statistical analysis t-test for unpaired differences (p) was used. Results expressed as mean values ± SEM:

	Controls	Classes I–IV	Class I	Class II	Class III	Class IV	DCM	VHD	CHD
bFGF	1.95±	5.69±	3.14±	3.74±	4.17±	8.09±	4.56±	4.76±	7.57±
(pg/ml)	0.33	0.79*	0.92	1.65	1.4*	1.32*	1.13*	1.22*	1.46*
ANG	249.8±	325.0±	237±	297.8±	319.2±	335.4±	320.3±	311.6±	336.8±
(ng/ml)	11.6	14.2*	21.2	34.6	23.6*	20.8*	27*	20.2*	23.8*

*$p < 0.05$ compared with controls

In conclusion, in end-stage HF patients there is a statistically significant increase in plasma levels of angiogenic factors bFGF and angiogenin. The progressive increase of plasma levels of bFGF and ANG suggest a dynamic continuous process possibly in neovascularisation. The clinical implication of this phenomenon in congestive HF needs further investigation.

1083-120 Cachexia in Chronic Heart Failure: Leptin Mediated Anorexia or Cytokine and Hormone Action?

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The cause of cardiac cachexia is not clear. The peptide leptin plays a role in obesity (leptin resistance), but also in weight loss during infection (leptin overexpression due to TNF-α and endotoxin action, subsequently anorexia). We aimed to relate body composition changes (dual x-ray absorptiometry, lean and fat tissue in relation to height) to cytokine, hormone, leptin, and soluble [s] CD14 levels (indicative of LPS cell interaction) in 48 CHF patients (age 61 ± 2y, LVEF 28 ± 2%, NYHA class 2.7 ± 0.1) and 21 healthy controls (57 ± 2y, p = 0.15). Leptin ($p < 0.02$), noradrenaline [NA], sTNF receptor 1, IL-6, sCD14 (all $p < 0.004$) and insulin ($p < 0.03$) were increased in CHF. Nineteen patients were cachectic ([c] dry weight loss 12 ± 2 kg over ≥ 6 months, particularly increased TNF-α, sTNF-R1, sCD14, and NA).